

A, Nogo B and part of Nogo C. The human Nogo amino acid sequence is depicted in Figure 13 and has been assigned SEQ ID NO:29.--

Please replace the present sequence listing with the substitute sequence listing enclosed herewith pursuant to 37 C.F.R. § 1.825.

IN THE CLAIMS:

A marked-up version of the amended claims is attached hereto as Exhibit A. Additions are shown by underlining and deletions are shown by brackets.

Please amend claim 11 to read as follows:

11. (amended) A protein comprising an amino acid sequence that has at least one conservative amino acid substitution in the amino acid sequence depicted in Figure 2a (SEQ ID NO:2), the amino acid sequence depicted in Figure 13 (SEQ ID NO:29) or the amino acid sequence depicted in Figure 14 (SEQ ID NO:32), and which is able to be bound by an antibody directed against a Nogo protein having an amino acid sequence selected from the group consisting of residues 1-1163 of SEQ ID NO: 2, residues 1-172 fused to 975-1163 of SEQ ID NO: 2, and residues 1-199 of SEQ ID NO: 32.

16. (amended) A purified protein comprising a fragment of a Nogo protein comprising an amino acid sequence selected from the group consisting of residues 31-57 depicted in Figure 2a (SEQ ID NO:2), the residues 11-191 depicted in Figure 14 (SEQ ID NO:32), the residues 988-1023 depicted in Figure 2a (SEQ ID NO:2), and residues 1090-1125 depicted in Figure 2a (SEQ ID NO:2), residues 994-1174 depicted in Figure 13 (SEQ ID NO:29), residues 977-1012 depicted in Figure 13 (SEQ ID NO:29), and residues 1079-1114 depicted in Figure 13 (SEQ ID NO:29).

30. (amended) An isolated nucleic acid comprising a nucleotide sequence encoding a protein comprising an amino acid sequence that has a greater than 50% homology to the amino acid sequence of SEQ ID NO:29, as determined by a BLAST computer algorithm.

52. (amended) A purified fragment of a Nogo protein comprising an amino acid sequence selected from the group consisting of amino acid residues 1-131, 132-939, 206-501, 501-680, 132-206, 680-939, and 940-1127 of SEQ ID NO:29, that is free of all central nervous system myelin material.

53. (amended) A purified fragment of a Nogo protein that lacks amino acid residues 132-206, amino acid residues 939-1127, or amino acid residues 132-206 and 939-1127, of SEQ ID NO:29 but otherwise comprises the remainder of SEQ ID NO:29, and that is free of all central nervous system myelin material.

55. (amended) A purified protein comprising a fragment of a Nogo protein, which protein (a) lacks amino acid residues 132-206, amino acid residues 939-1127, or amino acid residues 132-206 and 939-1127, of SEQ ID NO:29; and (b) displays the neurite growth inhibitory activity of said Nogo protein, and is free of all central nervous system myelin material.

58. (amended) An isolated nucleic acid that encodes a protein comprising an amino acid sequence selected from the group consisting of amino acid residues 1-131, 132-939, 206-501, 501-680, 132-206, 680-939, and 940-1127 of SEQ ID NO:29.


59. (amended) An isolated nucleic acid that encodes a protein that lacks amino acid residues 132-206, amino acid residues 939-1127, or amino acid residues 132-206 and 939-1127, of SEQ ID NO:29 but otherwise comprises the remainder of SEQ ID NO:29.

Please add the following new claims:

63. (new) A method of obtaining polyclonal antibodies to a protein, wherein said protein consists of an amino acid sequence with at least 60% identity to an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:29, SEQ ID NO:32, and SEQ ID NO:33 as determined by BLAST computer algorithm, and wherein said method comprises:

- (a) immunizing an animal with said protein that is free of all central nervous system myelin material with which said protein is natively associated; and,
- (b) recovering polyclonal antibodies from the animal.

64. (new) A method of obtaining polyclonal antibodies to a protein, wherein said protein consists of an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:29, SEQ ID NO:32 and SEQ ID NO:33, and wherein said method comprises:

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- (a) immunizing an animal with said protein or a derivative or a fragment thereof, said derivative or fragment consisting of at least 10 amino acids of said protein, that is free of all central nervous system myelin material with which said protein is natively associated; and,
 - (b) recovering polyclonal antibodies from the animal.

65. (new) The method of claim 64, wherein said derivative or fragment consists of at least 17 amino acids of said protein.

66. (new) The method of claim 64 wherein said derivative or fragment consists of an amino acid sequence selected from the group consisting of SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45 and SEQ ID NO:46.

67. (new) The method of claim 65, wherein said derivative or fragment consists of 18 amino acids of said protein.

68. (new) The method of claim 63 or 64, wherein said amino acid sequence is the amino acid sequence of SEQ ID NO:2.

69. (new) The method of claim 63 or 64 wherein said amino acid sequence is the amino acid sequence of SEQ ID NO:29.

70. (new) The method of claim 63 or 64 wherein said amino acid sequence is the amino acid sequence of SEQ ID NO:32.

71. (new) The method of claim 63 or 64 wherein said amino acid sequence is the amino acid sequence of SEQ ID NO:33.

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72. (new) The method of claim 64, wherein said derivative is a fusion protein, said fusion protein comprising (i) a first amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:29, SEQ ID NO:32, and SEQ ID NO:33 or a fragment of at least 10 amino acids of said first amino acid sequence; and (ii) a second amino acid sequence, different from said first amino acid sequence, that is covalently bound to said first amino acid sequence.

73. (new) The method of claim 72, wherein said fragment is a fragment of at least 17 amino acids of said first amino acid sequence.

74. (new) The method of claim 73, wherein said fragment consists of 18 amino acids of said first amino acid sequence.

75. (new) The method of claim 72, wherein said first amino acid sequence is the amino acid sequence of amino acids 762-1163 of SEQ ID NO:2.

76. (new) The method of claim 72, wherein said fragment consists of an amino acid sequence selected from the group consisting of SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45 and SEQ ID NO:46.

77. (new) The method of claim 64, wherein said fragment is a synthetic peptide.

78. (new) The method of claim 64, wherein said fragment consists of the amino acid sequence of amino acids 623-640 of SEQ ID NO:2.

79. (new) An isolated antiserum sample comprising polyclonal antibodies produced according to the method of any one of claims 63-78.

80. (new) A method of immunizing a non-human animal, said method comprising administering to said animal an immunogenic amount of a protein consisting of an amino acid sequence with at least 60% identity to an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:29, SEQ ID NO:32, and SEQ ID NO:33 as determined by BLAST computer algorithm, wherein said protein is free of all central nervous system myelin material with which said protein is natively associated.

81. (new) A method of immunizing a non-human animal, said method comprising administering to said animal an immunogenic amount of a protein consisting of an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:29, SEQ ID NO:32 and SEQ ID NO:33, and wherein said protein is free of all central nervous system myelin material with which said protein is natively associated.

82. (new) A method of immunizing a non-human animal, said method comprising administering to said animal an immunogenic amount of a derivative or a fragment of a protein consisting of an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:29, SEQ ID NO:32 and SEQ ID NO:33, and wherein said derivative or fragment (i) is free of all central nervous system myelin material with which said protein is natively associated; and (ii) consists of at least 10 amino acids of said protein.


83. (new) The method of claim 80, 81 or 82, wherein said animal is a mouse.

84. (new) The method of claim 82, wherein said fragment consists of at least 17 amino acids of said protein.

85. (new) The method of claim 84, wherein said fragment consists of 18 amino acids of said protein.

86. (new) The method of claim 82, wherein said fragment consists of an amino acid sequence selected from the group consisting of SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45 and SEQ ID NO:46.

87. (new) The method of claim 80, 81 or 82 wherein said amino acid sequence is the amino acid sequence of SEQ ID NO:2.

 88. (new) The method of claim 80, 81 or 82 wherein said amino acid sequence is the amino acid sequence of SEQ ID NO:29.

89. (new) The method of claim 80, 81 or 82 wherein said amino acid sequence is the amino acid sequence of SEQ ID NO:32.

90. (new) The method of claim 80, 81 or 82 wherein said amino acid sequence is the amino acid sequence of SEQ ID NO:33.

91. (new) The method of claim 80, 81 or 82 wherein said derivative is a fusion protein, said fusion protein comprising (i) a first amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:29, SEQ ID NO:32, and SEQ ID NO:33 or a fragment of at least 10 amino acids of said first amino acid sequence; and (ii) a second amino acid sequence, different from said first amino acid sequence, that is covalently bound to said first amino acid sequence.

92. (new) The method of claim 91, wherein said fragment is a fragment of at least 17 amino acids of said first amino acid sequence.

93. (new) The method of claim 92, wherein said fragment consists of 18 amino acids of said first amino acid sequence.



EXHIBIT B
PENDING CLAIMS AFTER ENTRY OF THE
AMENDMENT FILED APRIL 22, 2002
U.S. PATENT APPLICATION SERIAL NO. 09/830,972

1. A Nogo protein that is free of all central nervous system myelin material with which it is natively associated.
2. The protein of claim 1 which is selected from the group consisting of Nogo A and Nogo B.
3. The protein of claim 2 which comprises the amino acid sequence of Figure 2a (SEQ ID NO: 2).
4. The protein of claim 2, the amino acid sequence of which consists of an amino acid sequence selected from the group consisting of residues 1-1163 depicted in Figure 2a (SEQ ID NO: 2), and residues 1-172 fused to 975-1163 depicted in Figure 2 (SEQ ID NO: 2).
5. A purified Nogo C protein.
6. The protein of claim 5, which comprises the amino acid sequence of SEQ ID NO: 32 depicted in Figure 14.
7. The protein of claim 5, the amino acid sequence of which consists of SEQ ID NO: 32 depicted in Figure 14.
8. The protein of claim 2 or 5 which is recombinantly produced.
9. The protein of claim 2 or 5 which has the sequence of a mammalian protein.
10. The protein of claim 1, 2 or 5 which has the sequence of a human protein.

11. (amended) A protein comprising an amino acid sequence that has at least one conservative amino acid substitution in the amino acid sequence depicted in Figure 2a (SEQ ID NO:2), the amino acid sequence depicted in Figure 13 (SEQ ID NO:29) or the amino acid sequence depicted in Figure 14 (SEQ ID NO:32), and which is able to be bound by an antibody directed against a Nogo protein having an amino acid sequence selected from the group consisting of residues 1-1163 of SEQ ID NO: 2, residues 1-172 fused to 975-1163 of SEQ ID NO: 2, and residues 1-199 of SEQ ID NO: 32.

12. The protein of claim 1 which comprises an amino acid sequence that is displaying a greater than 50% homology to the amino acid sequence of SEQ ID NO:2, as determined by a BLAST computer algorithm.

13. The protein of claim 1 which is encoded by a first nucleic acid that is hybridizable to a second nucleic acid having the nucleotide sequence depicted in Figure 2a (SEQ ID NO:1) or the nucleotide sequence depicted in Figure 12 (SEQ ID NO:28).

14. A purified fragment of the protein of claim 1 which is able to be bound by an antibody directed against a Nogo protein, and wherein said purified fragment is free of all central nervous system myelin material.

15. A purified fragment of the protein of claim 5 or 11 which is able to be bound by an antibody directed against a Nogo protein.

16. (amended) A purified protein comprising a fragment of a Nogo protein comprising an amino acid sequence selected from the group consisting of residues 31-57 depicted in Figure 2a (SEQ ID NO:2), the residues 11-191 depicted in Figure 14 (SEQ ID NO:32), the residues 988-1023 depicted in Figure 2a (SEQ ID NO:2), and residues 1090-1125 depicted in Figure 2a (SEQ ID NO:2), residues 994-1174 depicted in Figure 13 (SEQ ID NO:29), residues 977-1012 depicted in Figure 13 (SEQ ID NO:29), and residues 1079-1114 depicted in Figure 13 (SEQ ID NO:29).

17. A purified unglycosylated protein which is selected from the group consisting of Nogo A, Nogo B and Nogo C.

18. A purified protein that is free of all central nervous system myelin material and that is encoded by a first nucleotide sequence that is hybridizable to a second nucleic acid, said second nucleic acid having a nucleotide sequence depicted in Figure 2a (SEQ ID NO:1) or a nucleotide sequence depicted in Figure 12 (SEQ ID NO:28), which protein is able to be bound by an antibody directed against a second protein having an amino acid sequence depicted in Figure 2a (SEQ ID NO:2).

19. A chimeric protein comprising a fragment of the protein of claim 2, 5, or 11 which is able to be bound by an antibody directed against a Nogo protein, fused by a covalent bond to at least a portion of a second protein, which said second protein is different from said fragment of protein of claim 2, 5, or 11.

20. A purified molecule comprising a fragment of the protein of claim 1 which is able to be bound by an antibody directed against a Nogo protein, and wherein said purified molecule is free of all central nervous system myelin material.

21. A purified molecule comprising a fragment of the protein of claim 5, or 11 which is able to be bound by an antibody directed against a Nogo protein.

22. An isolated nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:33.

23. An isolated nucleic acid comprising:

- (a) a nucleotide sequence that encodes a polypeptide having an amino acid sequence selected the group consisting of residues 1-1163 depicted in Figure 2a (SEQ ID NO:2), residues 1-172 fused to 975-1163 depicted in Figure 2a (SEQ ID NO:2), and residues 1-199 depicted in Figure 14 (SEQ ID NO:32); or

(b) the complement of the nucleotide sequence of (a).

24. An isolated first nucleic acid capable of hybridizing to a second nucleic acid, said second nucleic acid having a nucleotide sequence complementary to a nucleotide sequence that encodes a polypeptide having an amino acid sequence selected from the group consisting of residues 1-1163 depicted in Figure 2a (SEQ ID NO:2), residues 1-172 fused to 975-1163 depicted in Figure 2a (SEQ ID NO:2), and residues 1-199 depicted in Figure 14 (SEQ ID NO:32); and encodes a naturally occurring protein that is able to be bound by an antibody to a protein having an amino acid sequence of SEQ ID NO: 2.

25. The isolated nucleic acid of claim 24 which encodes a naturally occurring human Nogo protein.

26. An isolated first nucleic acid that is hybridizable to a second nucleic acid, said second nucleic acid having a nucleotide sequence depicted in Figure 2a (SEQ ID NO:1) or a nucleotide sequence depicted in Figure 12 (SEQ ID NO:28), and wherein said first nucleic acid encodes a first protein that is able to be bound by an antibody directed against a second protein having an amino acid sequence depicted in Figure 2a (SEQ ID NO:2).

27. An isolated nucleic acid that encodes a naturally occurring protein that is able to be bound by an antibody to a protein having an amino acid sequence of SEQ ID NO: 2, and that has a greater than 70% nucleotide sequence homology to a nucleotide sequence that encodes a polypeptide having an amino acid sequence selected from the group consisting of residues 1-1163 of SEQ ID NO:2, residues 1-172 fused to 975-1163 of SEQ ID NO:2, and residues 1-199 of SEQ ID NO:32, as determined by a BLAST computer algorithm.

28. The nucleic acid of claim 27 in which the naturally occurring protein is a human protein.

29. An isolated nucleic acid comprising a nucleotide sequence encoding a fragment of a Nogo protein that displays one or more functional activities of the Nogo protein, wherein

said Nogo protein is not a human Nogo protein, a *Drosophila* Nogo protein or a Nogo protein of *Caenorhabditis elegans*.

30. (amended) An isolated nucleic acid comprising a nucleotide sequence encoding a protein comprising an amino acid sequence that has a greater than 50% homology to the amino acid sequence of SEQ ID NO:29, as determined by a BLAST computer algorithm.

31. An isolated nucleic acid that encodes at least 220 continuous amino acid residues of the amino acid sequence of SEQ ID NO:2.

32. An isolated nucleic acid that comprises the nucleotide sequences of at least two non-overlapping human expressed sequence tags selected from the group consisting of: AA158636 (SEQ ID NO:35), AA333267 (SEQ ID NO:36), AA081783 (SEQ ID NO:37), AA167765 (SEQ ID NO:38), AA322918 (SEQ ID NO:39), AA092565 (SEQ ID NO:40), AA081525 (SEQ ID NO:41), and AA081840 (SEQ ID NO:42).

33. A vector comprising the nucleic acid of any one of claims 22, 23, 24, and 25 operably linked to a non-native promoter.

34. An expression vector comprising the nucleic acid of any one of claims 22, 23, 24, and 25.

35. A recombinant cell transformed with the nucleic acid of any one of claims 22, 23, 24, and 25.

36. The recombinant cell of claim 35 which is a prokaryotic recombinant cell.

37. The recombinant cell of claim 35 which is a eukaryotic recombinant cell.

38. A method of producing a recombinant protein comprising culturing a recombinant cell transformed with the nucleic acid of claim 22, 23, 24, or 25 such that a

protein encoded by the nucleic acid is expressed by the cell, and recovering the expressed protein.

39. The method of claim 38 wherein the recombinant cell is a prokaryotic recombinant cell.

40. The method of claim 38 wherein the recombinant cell is an eukaryotic recombinant cell.

41. A method of treating a subject with a neoplastic disease of the central nervous system comprising administering to the subject a therapeutically effective amount of a Nogo protein or a fragment thereof, that is free of all central nervous system myelin material with which the Nogo protein is natively associated, said fragment being active in inhibiting cell proliferation.

42. The method of claim 42 in which the neoplastic disease is glioma, glioblastoma, medulloblastoma, craniopharyngioma, ependyoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, meningioma, neuroblastoma, or retinoblastoma.

43. The method of claim 42 in which the subject is a human.

44. A method of treating a subject with damage to the central nervous system comprising administering to the subject a therapeutically effective amount of a ribozyme or an antisense Nogo nucleic acid that inhibits the production of Nogo in the subject.

45. A method of inducing regeneration or sprouting of neurons in a subject comprising administering to the subject a therapeutically effective amount of a ribozyme or an antisense Nogo nucleic acid that inhibits the production of Nogo in the subject.

46. A method of promoting structural plasticity of the central nervous system of a subject comprising administering to a subject in whom structural plasticity of the central

nervous system is desired a therapeutically effective amount of a ribozyme or an antisense Nogo nucleic acid that inhibits the production of Nogo in the subject.

47. A recombinant non-human animal that is the product of a process comprising introducing a nucleic acid encoding at least a domain of a Nogo protein into the genome of the animal, or a progeny of said animal.

48. A recombinant non-human animal in which a *Nogo* gene has been inactivated or deleted.

49. The animal of claim 48 in which the *Nogo* gene has been inactivated by a method comprising introducing a nucleic acid into the animal or an ancestor thereof, which nucleic acid comprises a non-Nogo gene sequence flanked by Nogo gene sequences that promote homologous recombination.

50. A purified fragment of a Nogo protein comprising an amino acid sequence selected from the group consisting of amino acid residues 1-171, 172-974, 259-542, 542-722, 172-259, 722-974, and 975-1162 of SEQ ID NO: 2, that is free of all central nervous system myelin material.

51. A purified fragment of a Nogo protein that lacks amino acid residues 172-259, amino acid residues 974-1162, or amino acid residues 172-259 and 974-1162, of SEQ ID NO:2 but otherwise comprises the remainder of SEQ ID NO: 2, and that is free of all central nervous system myelin material.

52. (amended) A purified fragment of a Nogo protein comprising an amino acid sequence selected from the group consisting of amino acid residues 1-131, 132-939, 206-501, 501-680, 132-206, 680-939, and 940-1127 of SEQ ID NO:29, that is free of all central nervous system myelin material.

53. (amended) A purified fragment of a Nogo protein that lacks amino acid residues 132-206, amino acid residues 939-1127, or amino acid residues 132-206 and 939-1127, of SEQ ID NO:29 but otherwise comprises the remainder of SEQ ID NO:29, and that is free of all central nervous system myelin material.

54. A purified protein comprising a fragment of a Nogo protein, which protein (a) lacks amino acid residues 172-259, amino acid residues 974-1162, or amino acid residues 172-259 and 974-1162, of SEQ ID NO:2; and (b) displays the neurite growth inhibitory activity of said Nogo protein, and is free of all central nervous system myelin material.

55. (amended) A purified protein comprising a fragment of a Nogo protein, which protein (a) lacks amino acid residues 132-206, amino acid residues 939-1127, or amino acid residues 132-206 and 939-1127, of SEQ ID NO:29; and (b) displays the neurite growth inhibitory activity of said Nogo protein, and is free of all central nervous system myelin material.

56. An isolated nucleic acid that encodes a protein comprising an amino acid sequence selected from the group consisting of amino acid residues 1-171, 172-974, 259-542, 542-722, 172-259, 722-974, and 975-1162 of SEQ ID NO: 2.

57. An isolated nucleic acid that encodes a protein that lacks amino acid residues 172-259, amino acid residues 974-1162, or amino acid residues 172-259 and 974-1162, of SEQ ID NO:2 but otherwise comprises the remainder of SEQ ID NO: 2.

58. (amended) An isolated nucleic acid that encodes a protein comprising an amino acid sequence selected from the group consisting of amino acid residues 1-131, 132-939, 206-501, 501-680, 132-206, 680-939, and 940-1127 of SEQ ID NO:29.

59. (amended) An isolated nucleic acid that encodes a protein that lacks amino acid residues 132-206, amino acid residues 939-1127, or amino acid residues 132-206 and 939-1127, of SEQ ID NO:29 but otherwise comprises the remainder of SEQ ID NO:29.

60. A vector comprising the nucleic acid of any one of claims 56, 57, 58 and 59.
61. A recombinant cell transformed with the nucleic acid of any one of claims 56, 57, 58 and 59.
62. A fusion protein comprising the fragment of claim 52, 53, or 55 fused to an amino acid sequence of a non-Nogo protein.
63. (new) A method of obtaining polyclonal antibodies to a protein, wherein said protein consists of an amino acid sequence with at least 60% identity to an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:29, SEQ ID NO:32, and SEQ ID NO:33 as determined by BLAST computer algorithm, and wherein said method comprises:
- (a) immunizing an animal with said protein that is free of all central nervous system myelin material with which said protein is natively associated; and,
 - (b) recovering polyclonal antibodies from the animal.
64. (new) A method of obtaining polyclonal antibodies to a protein, wherein said protein consists of an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:29, SEQ ID NO:32 and SEQ ID NO:33, and wherein said method comprises:
- (a) immunizing an animal with said protein or a derivative or a fragment thereof, said derivative or fragment consisting of at least 10 amino acids of said protein, that is free of all central nervous system myelin material with which said protein is natively associated; and,
 - (b) recovering polyclonal antibodies from the animal.
65. (new) The method of claim 64, wherein said derivative or fragment consists of at least 17 amino acids of said protein.

66. (new) The method of claim 64 wherein said derivative or fragment consists of an amino acid sequence selected from the group consisting of SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45 and SEQ ID NO:46.

67. (new) The method of claim 65, wherein said derivative or fragment consists of 18 amino acids of said protein.

68. (new) The method of claim 63 or 64, wherein said amino acid sequence is the amino acid sequence of SEQ ID NO:2.

69. (new) The method of claim 63 or 64 wherein said amino acid sequence is the amino acid sequence of SEQ ID NO:29.

70. (new) The method of claim 63 or 64 wherein said amino acid sequence is the amino acid sequence of SEQ ID NO:32.

71. (new) The method of claim 63 or 64 wherein said amino acid sequence is the amino acid sequence of SEQ ID NO:33.

72. (new) The method of claim 64, wherein said derivative is a fusion protein, said fusion protein comprising (i) a first amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:29, SEQ ID NO:32, and SEQ ID NO:33 or a fragment of at least 10 amino acids of said first amino acid sequence; and (ii) a second amino acid sequence, different from said first amino acid sequence, that is covalently bound to said first amino acid sequence.

73. (new) The method of claim 72, wherein said fragment is a fragment of at least 17 amino acids of said first amino acid sequence.

74. (new) The method of claim 73, wherein said fragment consists of 18 amino acids of said first amino acid sequence.

75. (new) The method of claim 72, wherein said first amino acid sequence is the amino acid sequence of amino acids 762-1163 of SEQ ID NO:2.

76. (new) The method of claim 72, wherein said fragment consists of an amino acid sequence selected from the group consisting of SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45 and SEQ ID NO:46.

77. (new) The method of claim 64, wherein said fragment is a synthetic peptide.

78. (new) The method of claim 64, wherein said fragment consists of the amino acid sequence of amino acids 623-640 of SEQ ID NO:2.

79. (new) An isolated antiserum sample comprising polyclonal antibodies produced according to the method of any one of claims 63-78.

80. (new) A method of immunizing a non-human animal, said method comprising administering to said animal an immunogenic amount of a protein consisting of an amino acid sequence with at least 60% identity to an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:29, SEQ ID NO:32, and SEQ ID NO:33 as determined by BLAST computer algorithm, wherein said protein is free of all central nervous system myelin material with which said protein is natively associated.

81. (new) A method of immunizing a non-human animal, said method comprising administering to said animal an immunogenic amount of a protein consisting of an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:29, SEQ ID NO:32 and SEQ ID NO:33, and wherein said protein is free of all central nervous system myelin material with which said protein is natively associated.

82. (new) A method of immunizing a non-human animal, said method comprising administering to said animal an immunogenic amount of a derivative or a fragment of a protein consisting of an amino acid sequence selected from the group consisting

of SEQ ID NO:2, SEQ ID NO:29, SEQ ID NO:32 and SEQ ID NO:33, and wherein said derivative or fragment (i) is free of all central nervous system myelin material with which said protein is natively associated; and (ii) consists of at least 10 amino acids of said protein.

83. (new) The method of claim 80, 81 or 82, wherein said animal is a mouse.

84. (new) The method of claim 82, wherein said fragment consists of at least 17 amino acids of said protein.

85. (new) The method of claim 84, wherein said fragment consists of 18 amino acids of said protein.

86. (new) The method of claim 82, wherein said fragment consists of an amino acid sequence selected from the group consisting of SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45 and SEQ ID NO:46.

87. (new) The method of claim 80, 81 or 82 wherein said amino acid sequence is the amino acid sequence of SEQ ID NO:2.

88. (new) The method of claim 80, 81 or 82 wherein said amino acid sequence is the amino acid sequence of SEQ ID NO:29.

89. (new) The method of claim 80, 81 or 82 wherein said amino acid sequence is the amino acid sequence of SEQ ID NO:32.

90. (new) The method of claim 80, 81 or 82 wherein said amino acid sequence is the amino acid sequence of SEQ ID NO:33.

91. (new) The method of claim 80, 81 or 82 wherein said derivative is a fusion protein, said fusion protein comprising (i) a first amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:29, SEQ ID NO:32, and SEQ ID NO:33 or a

fragment of at least 10 amino acids of said first amino acid sequence; and (ii) a second amino acid sequence, different from said first amino acid sequence, that is covalently bound to said first amino acid sequence.

92. (new) The method of claim 91, wherein said fragment is a fragment of at least 17 amino acids of said first amino acid sequence.

93. (new) The method of claim 92, wherein said fragment consists of 18 amino acids of said first amino acid sequence.

94. (new) The method of claim 91, wherein said fragment consists of an amino acid sequence selected from the group consisting of SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, and SEQ ID NO:46.

95. (new) The method of claim 91, wherein said first amino acid sequence is the amino acid sequence of amino acids 762-1163 of SEQ ID NO:2.

96. (new) The method of claim 82, wherein said fragment is a synthetic peptide.

97. (new) The method of claim 82, wherein said fragment consists of the amino acid sequence of amino acids 623-640 of SEQ ID NO:2.